IMPACT OF FUEL CHOICE ON COMPARATIVE CANCER RISK OF EMISSIONS

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ABSTRACT

Incomplete combustion of fuels as an energy source results in the emission of products which are mutagenic in short-term genetic bioassays and carcinogenic in animals. Humans occupationally exposed to the incomplete combustion products from certain fuels have an elevated relative risk of cancer. Until recently, it has not been possible to compare the relative cancer risk of emissions from the combustion of various fuels. The combustion emissions from a wide variety of fossil fuels, synthetic fuels, vegetative fuels, synthetic chemicals, and mixed wastes have been characterized for with respect to their comparative genotoxic and tumor initiating activity. This paper evaluates the comparative cancer risk of various fuels in our current data base and identifies critical data gaps in our understanding of the comparative cancer risks from using alternative fuels.

INTRODUCTION

Fossil fuel related mixtures were the first chemicals recognized as human and then animal carcinogens (1). Coal combustion products, chimney soots, and coal tars were the first fossil fuel derived chemical carcinogens studied. Evaluation of the weight of evidence for the carcinogenic risk to humans of many fuel related mixtures has been conducted by the International Agency for Research on Cancer (IARC)(2). Based on these evaluations soots, coal-tars, and shale oils are classified as carcinogenic to humans (Group 1). Carcinogenicity in animals, with limited evidence in humans, has led to diesel engine exhaust and occupational exposures in petroleum refining to be classified as probably carcinogenic to humans (Group 2A). For several other petroleum based fuels (e.g., unleaded gasoline, marine diesel fuel, and residual fuel oils) and their combustion products (e.g., gasoline engine exhaust) the IARC has classified these mixtures as possibly carcinogenic to humans (Group 2B) based principally on the evidence for carcinogenicity in animal studies. Clearly, human exposure to a number of fossil fuel products, especially the combustion products, presents a potential cancer risk.

Vegetative carbon, from non-fossilized plants, was probably the first carbon source used as a fuel. Unfortunately, with the exception of tobacco combustion products, few studies have been conducted to evaluate the human cancer risk from vegetative carbon sources. A lung cancer mortality study in China in a non-smoking female population exposed to high concentrations of indoor burning of either "smoky" coal, "smokeless coal" or wood show that the lung

cancer mortality rates are highest in the populations using the smoky coal (3).

Alternative coal and shale derived fuels and products associated with technologies such as coal liquefaction were evaluated for genotoxicity, carcinogenicity, and other toxicological effects by industry and the U.S. Dept. of Energy (4). In many cases these alternative "synfuels" were compared to conventional petroleum-based fuels. No studies have been conducted on the cancer risk from alternative fuels such as synthetic chemical fuels, oxygenated petroleum fuels and alcohol based fuels.

HUMAN EXPOSURE

The most significant human exposures from fuel use are the air pollution exposures resulting from fuel related combustion emissions from transportation, heating and other area sources (5). Combustion emissions are a complex mixture of gases, condensable organics, and particles. The particles vary from classical submicron carbonaceous soot particles with condensed organics, and inorganic particulate matter to a mixture of condensable organic matter with almost no carbonaceous soot. The condensed or adsorbed organic, often referred to as "tar" in the earlier literature contains the polycyclic organic matter (POM) which induces tumors in animals, mutations in cells, and has been clearly implicated in epidemiological studies as a human carcinogen (5,6).

Polycyclic organic matter (POM) is a general term referring to a complex organic mixture of polycyclic aromatic compounds including many diverse classes of hydrocarbons (e.g. polycyclic aromatic hydrocarbons, PAH), substituted aromatic hydrocarbons (e.g., nitrated-PAH), heterocyclic aromatic compounds (e.g., aza-arenes). Incomplete combustion products, however, also contain gaseous chemicals which are carcinogenic such as benzene, aldehydes, and alkenes (e.g., 1,3-butadiene) and semi-volatile organic compounds which have not been well characterized either chemically or toxicologically (6).

The complexity of the POM emissions, estimated to contain thousands of chemicals, has precluded the quantitative cancer risk assessment of these emissions based on analysis of the components. Since human exposure to these POM emissions occurs as the whole complex mixture, both qualitative, weight of evidence, assessments (2) and quantitative assessments (7) of the human cancer risks have been based on either the whole emissions or the POM component.

CANCER POTENCY AND RISK

Three different approaches have been taken to the quantitative assessment of human cancer risk from fuel related mixtures: 1.Low dose extrapolation of human cancer risks at relatively higher occupational exposures (8), 2.Extrapolation of chronic animal cancer studies to human risk using cross species extrapolation methods (7) and 3.Extrapolation from relative tumor potency data in animals to relative cancer risk in humans based on the comparative

potency method. The first method, relying only on human data, has been the most extensively used for fuel related mixtures (e.g., coke oven emissions (8)), however there is not adequate human data to assess the potential cancer impact of either the currently used conventional fuels (e.g., petroleum derived) or the possible alternative fuels that may be used in the future. The second method, relying on chronic animal cancer data, is also severely limited by the available chronic animal data. The third method, relies on a comparative potency data base for a series of combustion related POM mixtures which have been compared in animal tumor assays and short-term bioassays to the relative human lung cancer risk in a series of related POM mixtures.

The comparative potency method for cancer risk assessment of these complex POM emissions is based on the constant relative potency hypothesis. This method was developed and tested using human lung cancer unit risk estimates, animal tumorigenicity data, and short-term mutagenesis bioassay data (9,10) These mixtures included the extractable organic emissions from coke ovens, roofing coal tar pots, cigarette smoke and automotive emissions. The comparative potency method is based on the hypothesis that there is a constant relative potency between two different carcinogens across human and bioassay data. The mathematical expression for the constant relative potency model is the following:

$$\frac{bioassay\ potency\ of\ \dfrac{carcinogen_\alpha}{carcinogen_\beta}}{human\ cancer\ potency\ of\ \dfrac{carcinogen_\alpha}{carcinogen_\beta}} = (k)\ constant$$

The constant relative potency assumption is implicit in any comparison which utilizes the relative toxicity of two substances in animals to estimate their relative toxicity in humans. This constant relative potency assumption is an experimentally testable hypothesis, if the relative potency of two mixtures or components in one bioassay (e.g., humans) can be determined and compared to the relative potency in a second bioassay. The test of this hypothesis is whether there is a constant relationship (k) between the relative potencies in the two bioassay being compared.
This hypothesis was tested for three complex organic emissions from a coke oven, roofing coal tar pot and cigarettes by using the human lung cancer data from epidemiological studies of humans exposed to these emissions and comparing the lung cancer unit risk to the potency of these emission sources in a series of bioassays (7,8).

The first application of this method to estimation of the human lung cancer unit risk was for the POM associated with diesel particle emissions (9). In this study, the comparative human data used was for POM from coke ovens, roofing coal tar emissions and cigarette smoke. Evaluation of a battery of bioassay demonstrated that across these three human carcinogens, the constant relative

potency hypothesis could be validated for the mouse skin tumor initiation potency. This is shown in Table 1 by the correlation between the human lung cancer unit risk and the tumor initiation potency for the three human carcinogens.

Table 1.
CANCER UNIT RISK ESTIMATES FOR THE HUMAN COMPARATIVE EMISSIONS

EMISSION SOURCE	HUMAN CANCER POTENCY[a] lifetime risk/ug EOM/m3	TUMOR POTENCY[b] pap/mouse/mg EOM
Coke Oven	$9.3 \times 10-4$ $(1.0)^{c}$	2.1 (1.0)
Roofing Tar (Coal)	$3.6 \times 10-4$ (0.39)	0.41 (0.2)
Cigarette Smoke	$2.2 \times 10-6$ (0.0024)	0.0024(0.0011)

[a]Lifetime cancer unit risk per microgram extractable organic matter (EOM) per cubic meter determined from human epidemiological data(9) [b]Papillomas per mouse per mg of EOM [c]Relative potency shown in ().

Using this methodology the lung cancer unit risk has been estimated for the following POM emission sources as shown below:

Table 2:
CANCER UNIT RISK ESTIMATES DETERMINED BY THE COMPARATIVE POTENCY METHOD[a]

EMISSION SOURCE	POM UNIT RISK (lifetime risk/ug organic matter/m3)	PARTICLE UNIT RISK (lifetime risk/ug particulate matter/m3)
Automobile-Gasoline Catalyst Non-catalyst	12.0×10^{-5}	5.1×10^{-5} 1.6×10^{-5}
Automobile-Diesel[b] Trucks-Diesel	23.0×10^{-5} 0.7×10^{-5}	2.6×10^{-5} 0.2×10^{-5}
Woodstoves	2.9×10^{-5}	1.0×10^{-5}
Heating Fuel Oil		0.9×10^{-5}

[a]Mouse skin tumor initiation bioassay potency was used as the comparative bioassay.
[b]Average of the unit risk estimate for three light-duty diesel vehicles(9).

The validity of this constant relative potency hypothesis may

depend on the chemical nature of the mixtures being compared as
well as the similarity of those mixtures.   Comparison of the
mutagenic potency of a series of POM from diesel and gasoline
vehicle emissions in Salmonella typhimurium with the tumorigenic
potency showed high correlations both between the two bioassay and
with the concentration of nitrated PAH and PAH in the POM mixture
(11).

IMPACT ANALYSIS OF CANCER RISK

Human cancer risk from exposure to a fuel or it's combustion
products is dependent on the extent of exposure (e.g., dose or
exposure concentration x time of exposure) and the potency of the
carcinogen (e.g., cancer risk/unit dose) among other factors (e.g.,
individual susceptibility). It is important to develop tools to
predict the potential impact of cancer risk in the absence of human
exposure assessment data so that such assessments can be conducted
prior to the widespread introduction of new fuels or technologies
into commerce.   By combining source emission studies with
mutagenicity and tumorigenicity bioassay studies of the combustion
source emissions, we are able to estimate the relative impact of
various alternative fuels as shown in Table 3.

Table 3.
COMPARATIVE MUTAGENIC AND TUMORIGENIC EMISSION FACTORS

SOURCE	MUTAGENIC EMISSION FACTOR (rev/kg fuel x 10^5)[a]	TUMORIGENIC EMISSION FACTOR (pap/mouse/kg fuel)[b]
RESIDENTIAL HEATING		
wood	50	83
oil	1	3
AUTOMOTIVE SOURCES		
diesel vehicles	40	240
gasoline non-catalyst	10	20
gasoline catalyst	1	2

[a]Revertants (rev) measured using the Salmonella typhimurium
mutagenicity bioassay
[b]Papillomas (pap) measured using the mouse skin tumor bioassay

This analysis of the potential impact of sources based on the
relative bioassay potency expressed per kg fuel consumption shows
even more clearly the comparative differences between these fuels
and sources.   In this analysis the potential human exposure is
assumed to be directly related to the emission rate. Although wood
combustion emissions are less potent as carcinogens than many of
fossil fuel combustion emissions, the high organic emission rate of
woodstoves results in a significant impact when both potential
exposure and potency are combined.

To examine the impact of fuel within one combustion source, we have conducted fuels comparison studies by operating motor vehicles, with different qualities and sources of diesel fuels. In several independent studies of diesel fuels we consistently found that alterations in the combustion source (engine type or operating conditions) resulted in greater differences in the mutagenic emission rates that differences in fuel quality or source (e.g. shale derived vs petroleum) (12).

Unfortunately few such fuel comparison studies have been conducted with gasoline vehicles, residential heating sources, waste burning and other significant fuel combustion sources. New oxygenated fuels being widely introduced into vehicle fleets across urban areas are expected to result in reduced POM emissions and reduced risk. However, no studies of the potential genotoxicity or tumorigenicity of these emissions have be conducted. The combustion of synthetic chemicals such as plastics mixed in municipal and hospital wastes and hazardous waste is the least well characterized with respect to the biological activity or potential cancer impact of the complex mixtures emitted from these sources.

DISCLAIMER
The research described in this paper has been reviewed by the US EPA and approved for scientific publication. The contents do not necessarily reflect the views and policies of the Agency.

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